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Hoechst

R 14



Hoechst Aktiengesellschaft
Pharma Research
Toxicology

20th December 1977

Mucosal tolerance to
Ma Ref 03801
in the rabbit
Report No. 1128/77

Summary

Under the test conditions described, Ma Ref 03801 can be regarded as having a slight irritant effect on mucous membranes.

Ma Ref 03801 = Shampoo
without Octopirox

/2

3177-7119

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Scale for Scoring Ocular Lesions

(1) Cornea		
(A) Opacity-degree of density (area most dense taken for reading)		
No Opacity	0	
Scattered or diffuse area, details of iris clearly visible	1	
Easily discernible translucent areas, details of iris slightly obscured.....	2	
Opalescent areas, no details of iris visible, size of pupil barely discernible.....	3	
Opaque, iris invisible.....	4	
(B) Area of cornea involved		
One quarter (or less) but not zero.....	1	
Greater than one quarter, but less than half.....	2	
Greater than half, but less than three quarters.....	3	
Greater than three quarters, up to whole area.....	4	
A X B X 5	Total maximum = 80	
(2) Iris		
(A) Values		
Normal.....	0	
Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof) iris still reacting to light (sluggish reaction is positive).....	1	
No reaction to light, hemorrhage, gross destruction (any or all of these).....	2	
A X 5	Total maximum = 10	
(3) Conjunctivae		
(A) Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris)		
Vessels normal.....	0	
Vessels definitely injected above normal.....	1	
More diffuse, deeper crimson red, individual vessels not easily discernible...	2	
Diffuse beefy red.....	3	
(B) Chemosis		
No swelling.....	0	
Any swelling above normal (includes nictitating membrane).....	1	
Obvious swelling with partial eversion of lids.....	2	
Swelling with lids about half closed.....	3	
Swelling with lids about half closed to completely closed.....	4	
(C) Discharge		
No discharge.....	C	
Any amount different from normal (does not include small amounts observed in inner canthus of normal animals).....	1	
Discharge with moistening of the lids and hairs just adjacent to lids.....	2	
Discharge with moistening of the lids and hairs, and considerable area around around the eye.....	3	
Score (A + B + C) X 2	Total maximum = 20	

The scores for cornea (1), iris (2), and conjunctivae (3) obtained in each rabbit at the specific reading time are added to give the primary irritation score. The mean of the scores for all rabbits at the specific reading time is calculated. The highest score obtained at any of the reading times is used for the evaluation and the substance is categorized as follows:

0 - 10	Non-irritant	(nicht reizend)
11 - 25	Slightly irritant	(leicht reizend)
26 - 56	Moderately irritant	(mäßig reizend)
57 - 110	Severely irritant	(stark reizend)

Hoechst

Schleimhautverträglichkeit / Eye irritation

Substanz / Substance Ma Ref 03801		Konzentration / Concentration diluted 1:1 with water								Dosis / Dose 0,1 ml						Tierart / Species Albino Himalayan rabbit																
Zeit / Time		10'				60'				180'				330'				24 h														
+ = rinsed																																
Kaninchen Nr. / out after 1'	Rabbit No.	+	+	+	82	83	84	85	86	87	82	83	84	85	86	87	82	83	84	85	86	87										
I Cornea	A Grad der Trübung / Opacity	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	0	1									
B Betroffener Bereich / Area involved	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	2	1	2	0	1							
a - A x B x 5 (max. 80)	0	0	0	0	0	0	0	0	5	5	5	5	0	5	5	5	5	0	10	5	5	5	5	10	5	10	0	5				
II Iris	Bewertung / Value	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
b - Wert x 5 (max. 10)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
III Conjunctiva	A Rötung / Redness	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2	2	2	1	1	2	2	2	2	2	2	2	1	1	2		
B Schwellung / Chemosis	0	0	1	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1		
C Absonderungen / Discharge	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1	1	2	2	2	0	0	2	2	1	1	0	0	2	0	0
c - (A + B + C) x 2 (max 20)	2	2	4	2	2	4	4	4	4	4	4	4	4	4	8	8	8	10	8	12	4	4	10	10	8	8	6	6	10	4	4	
a + b + c (max. 110)	2	2	4	2	2	4	4	9	9	9	4	9	13	13	13	15	8	22	9	9	15	15	13	18	11	16	15	14	4	11		
\bar{x}		3	3		7		7				13		13		15		15		11		15		14		10							
\bar{x}		3			7		7								14				13					12								



Schleimhautverträglichkeit / Eye irritation

Substanz / Substance Ma Ref 03801		Konzentration / Concentration diluted 1:1 with water						Dosis / Dose 0,1 ml		Tierart / Species Albino Himalayan rabbit							
Zeit / Time		48 h			72 h												
+ = rinsed																	
Kaninchen Nr. / out after 1'	Rabbit No.	+	+	+	82	83	84	85	86	87	82	83	84	85	86	87	
A Grad der Trübung / Opacity		1	1	1							+	0	0	0	0	0	1
I Cornea	B Betroffener Bereich / Area involved	1	1	1	1	0	1					0	0	0	0	0	1
a - A x B x 5 (max. 80)		5	5	5	5	0	5				died	0	0	0	0	0	5
II Iris	Bewertung / Value	0	0	0	0	0	0				72 h post	0	0	0	0	0	0
b - Wert x 5 (max. 10)		0	0	0	0	0	0				appl.	0	0	0	0	0	0
III Con-junctiva	A Rötung / Redness	1	1	1	1	0	1				0	0	1	0	1		
B Schwellung / Chemosis		0	0	0	0	0	0				0	0	0	0	0	0	
C Absonderungen / Discharge		0	0	0	0	0	0				0	0	0	0	0	0	
c - (A + B + C) x 2 (max 20)		2	2	2	2	0	2				0	0	2	0	2		
a + b + c (max 110)		7	7	7	7	0	7				0	0	2	0	7		
X											3						
X											6						

Implementation of the Trial

We tested mucosal tolerance to Ma Ref 03801 in six albino Himalayan rabbits by a single application of 0.1 ml of a 1 : 1 dilution of the preparation in water into the conjunctival sac of the rabbits' left eyes. 0.1 ml of water was applied into the conjunctival sac of the right eyes as a control. Both eyes of three of the six treated animals were cleansed one minute after application, using 20 ml of water in each case. Warm tap water (37 °C) with a pH value of 7.3 and a degree of hardness of 21 °dH [deutsche Härtegrad = German degree of hardness] was used for rinsing out the eyes.

The results were assessed with the aid of a magnifying glass 10, 60 180 and 330 minutes after treatment and also after 24, 48 and 72 hours. The 24, 48 and 72-hour findings were obtained following instillation of one drop of fluorescein sodium in a 1 : 10 000 dilution = 0.01 %. Once these assessments had been completed, the treated eyes were rinsed out with physiological saline solution.

The trial was performed during the period between the 5th and the 8th December 1977.

Results:

Under the above-mentioned test conditions, the peak irritant indices of Ma Ref 03801 were found to be:

- 14 in cleansed eyes after 24 hours;
- 15 in uncleansed eyes after 180 or 330 minutes;
- 14 as the mean value in all animals after 180 minutes.

Thus, Ma Ref 03801 can be regarded as having a slight irritant effect on mucous membranes.

Dr. Ma/Ju
20th December 1977

Pharma Research
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Appendix

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**EVALUATION OF CORNEA AFTER INSTILLATION OF ONE DROP
FLUORESCEIN SODIUM 0.01 %**

Substance:	Concentration:	Dose:	Species:					
Ma Ref 03801	diluted with water 1 : 1	0,1 ml	Albino Himalayan rabbit					
Time:	Opaque area of the cornea							
	Rabbit No.:							
	82	83	84	85	86			
24 hours after appl.	2/3	1/3	1/2	1/2	*			
					1/2			
48 hours after appl	1/3	NAD	*	*	NAD			
					1/8			
72 hours after appl.	NAD	NAD	NAD	NAD	NAD			
Remark: *punctiform, pinhead-sized opacity of the cornea								

Substance:	Concentration:	Dose:	Species:					
water (control eye)		0,1 ml	Albino Himalayan rabb					
Time:	Opaque area of the cornea							
	Rabbit No.:							
	82	83	84	85	86			
24 hours after appl.	NAD	NAD	NAD	NAD	NAD			
					NAD			
48 hours after appl.	NAD	NAD	NAD	NAD	NAD			
					NAD			
72 hours after appl.		NAD	NAD	NAD	NAD			
Remark: *punctiform, pinhead-sized opacity of the cornea								